

REMARKS

The claims have been amended to require the presence of hydroquinone. Support for these amendments exists throughout the entire specification.

Claim 23 has been canceled.

Claims 1-22 are currently pending.

The Office Action rejected claims 1-22 under 35 U.S.C. § 103 as obvious over WO 99/10318 ("Phillippe"). The Office Action also rejected claims 1-22 under the judicially created doctrine of obviousness-type double patenting over Phillippe's corresponding U.S. patent application. In view of the following comments, Applicants respectfully request reconsideration and withdrawal of these rejections.

The only rejections in this case are based on the assertion that the claimed combination of compounds would have been obvious over Phillippe. Nothing in Phillippe teaches or suggests the claimed, synergistic combination of specific compounds. However, even assuming Phillippe renders the claimed invention *prima facie* obvious --which it does not-- Applicants' showing of synergism is more than sufficient to rebut any such hypothetical case of *prima facie* obviousness.

The claimed invention relates to the specific, synergistic combination of N-cholesteryloxycarbonyl-4-para-aminophenol and hydroquinone. As demonstrated in the examples in the present application as well as further testing discussed herein, this specific

Application No. 09/784,179
Response to Office Action dated May 18, 2004

combination of compounds results in synergistic anti-depigmentation activity, a result which is “unexpected and surprising.”

In fact, the Office Action dated April 23, 2003, admitted that Applicants’ data submitted up to that point in time “convincingly demonstrate[s] the unexpected result” of the N-cholesteryloxy carbonyl-4-para-aminophenol/hydroquinone combination at particular concentrations. However, the Office Action questioned whether the unexpected results were commensurate in scope with the claims.

Submitted concurrently herewith is a new Rule 132 declaration demonstrating such synergism is commensurate in scope with the claims. This declaration demonstrates that the claimed combination of hydroquinone and N-cholesteryloxy carbonyl-4-para-aminophenol results in synergistic inhibition activity at different hydroquinone concentration levels. (Rule 132 declaration, pars. 3 and 4). Specifically, for hydroquinone concentrations of 4×10^{-5} M, the actual inhibition was 21.35% (as opposed to 16.03% theoretical). (Rule 132 declaration, par. 4). For hydroquinone concentrations of 12×10^{-5} M, the actual inhibition was 63.55% (as opposed to 55.90% theoretical). (Rule 132 declaration, par. 4). This information, combined with the data set forth in the present application and the Rule 132 declaration submitted April 23, 2003, demonstrate that the claimed combination of hydroquinone and N-cholesteryloxy carbonyl-4-para-aminophenol results in synergistic inhibition activity at different hydroquinone concentration levels,

Application No. 09/784,179
Response to Office Action dated May 18, 2004

and, necessarily, different hydroquinone/N-cholesteryloxy carbonyl-4-para-aminophenol ratios (Rule 132 declaration, par. 5).

Moreover, the declaration indicates that there is no reason to believe that such synergistic inhibition activity would not also be achieved using untested different concentration levels of N-cholesteryloxy carbonyl-4-para-aminophenol. (Rule 132 declaration, par. 5). Thus, the declaration demonstrates that the synergism associated with the claimed invention is commensurate in scope with the claims.

The declaration goes on to note that in the April 23, 2003, declaration, the combination of hydroquinone and a different aminophenol derivative, N-ethyloxy carbonyl-4-paraaminophenol, did not result in synergistic inhibition activity and, in fact, resulted in less than additive activity (16.48% actual inhibition vs. 39.76% theoretical). (Rule 132 declaration, par. 6). The declaration then explains that the difference in inhibition activity between the claimed hydroquinone/N-cholesteryloxy carbonyl-4-para-aminophenol combination and the comparative combination was unexpected and surprising, and demonstrates the improved depigmentating activity of the synergistic combination of the claimed invention. (Rule 132 declaration, par. 7).

Clearly, all of the data and other information set forth in the Rule 132 declarations submitted in this case as well as the present application demonstrates that the specific combination of compounds required by the present invention possess synergistic anti-

Application No. 09/784,179
Response to Office Action dated May 18, 2004

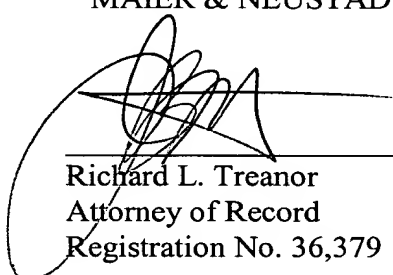
depigmentation activity.

In view of the above, Applicants respectfully submit that the examples in the present application as well as the testing discussed above are more than sufficient to demonstrate the novel, non-obvious, synergistic nature of the claimed combinations of compounds. Accordingly, Applicants respectfully submit that the pending rejections based upon Phillippe be withdrawn.

Applicants believe that the present application is in condition for allowance. Prompt and favorable consideration is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.



Richard L. Treanor
Attorney of Record
Registration No. 36,379

Jeffrey B. McIntyre
Registration No. 36,867

Customer Number

22850

Tel #: (703) 413-3000
Fax #: (703) 413-2220